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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,306	12/08/2000	Margaret A. Schwarz	9022.20	3192

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EXAMINER
EPPS FORD, JANET L

ART UNIT	PAPER NUMBER
1633	

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01/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/733,306	SCHWARZ, MARGARET A.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-14,16-19 and 47-57* is/are pending in the application.

4a) Of the above claim(s) *55-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-14,16-19 and 47-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1-4, 6-14, 16-19, and 47-57 are presenting pending for examination.

3. Newly submitted claims 55-57 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 55-57 are directed to methods comprising the administration of an antibody targeting SEQ ID NO: 1. First it is noted that SEQ ID NO: 1 is not a fragment of SEQ ID NO: 4 such that the prior search of SEQ ID NO: 4 would have co-extensive in scope with SEQ ID NO: 1. Therefore a new search of the prior art would be required to examine these new claims. Moreover, a search of antibodies targeting the amino acid sequence of SEQ ID NO: 1 would not encompass those antibodies targeting SEQ ID NO: 4. Therefore, the claims directed to the use of antibodies targeting SEQ ID NO: 1 are considered to be drawn to a patentably distinct method from the claims directed to a method comprising the administration of an antibody targeting SEQ ID NO: 4.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 55-57 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Specification

4. The objection to the specification as recited in the prior Office Action is withdrawn in response to Applicants amendment to the specification filed 10/25/07.

Claim Rejections - 35 USC § 112

5. Claims 1-4, 6-14, and 16-19 remain rejected and new claims 47-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention., for the reasons of record.

6. Applicant's arguments filed 10/25/07 have been fully considered but they are not persuasive.

7. Applicants traverse the instant rejection on the grounds that there is no evidence that undue experimentation would be required to practice the invention as claimed without having detailed knowledge of the *in vivo* processing of EMAP II. The arguments of counsel cannot take the place of evidence in the record. (See MPEP § 716.01(c)[R-2]). Moreover, once reasonable basis for questioning the adequacy of the disclosure has been advanced, it becomes incumbent on the applicant to rebut that challenge and factually demonstrate that his or her application disclosure is in fact sufficient. Applicants have merely dismissed the examiners citation of multiple references that suggest that (1) the biologically active form of EMAP II was uncertain as of the filing date of the instant application, (2) the further experimentation was required to

understand its role *in vivo,* and (3) that experimental data based upon the use of antibodies targeting a peptide fragment that is not found in SEQ ID NO: 4, is not sufficient to provide sufficient guidance to practice the full scope of the claimed invention.

8. Contrary to Applicant's assertions, the disclosure of the *in vivo* use of antibodies targeting an amino acid sequence that is distinct from SEQ ID NO: 4, namely SEQ ID NO: 1, is not sufficient to provide predictive guidance for the use of antibodies targeting SEQ ID NO: 4 *in vivo.* Moreover in regards to the having knowledge of the *in vivo* processing of EMAP II, it is unclear how it is possible to know what form of EMAP II would be present in diseased adult cardiac muscle such that administration of an antibody targeting the biologically active form of EMAP II would effectively block its function such that vessel formation could be facilitated. Applicants have not provided any evidence that EMAP II having the sequence of SEQ ID NO: 4 is expressed in human adult diseased cardiac tissue such that inhibition of EMAP II function via antibody administration would effectively facilitate vessel formation in the cardiac tissue such that amelioration of the diseased state in the human would be achieved.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. As stated in the prior Office Action, as of the filing date of the instant application further experimentation was required to identify the biologically active form of EMAP II. In regards to the state of the prior art as of the filing date of the instant specification, the exact structure and function of EMAP II *in vivo* was

unknown, as evidenced by Murray et al. (American Journal of Pathology, Vol. 157, No. 6, 2000, pages 2045-2053), and there was no guidance or teaching for the using the full scope of antibodies targeting mature EMAP II or a precursor EMAP II for the facilitation of vascular growth in cardiac muscle of a human subject afflicted with myocardial ischemia, atherosclerosis, myocardial disease, cardiomyopathy or cardiac hypertrophy, particularly for the treatment of these diseases. Therefore, Applicant's claim to methods comprising the use of antibodies targeting EMAP II of SEQ ID NO: 4, or a precursor comprising SEQ ID NO: 4 were not known as of the filing date of the instant invention. Murray et al. further note that the distribution of the EMAP II protein *in vivo* was not known prior to their studies (see page 2046, 4th paragraph). Immunohistochemical analysis of EMAP II distribution revealed occasional weak cytoplasmic staining of endothelial cells in lung, heart, cervix, ovary, and small and large intestine, although in general blood vessels of all sizes were negative. *In the heart there was weak cytoplasmic staining of muscle*, with darker staining of some capillaries (see page 2049, paragraph 3).

Furthermore, the teachings of Schwarz et al. (1999) did not demonstrate a clear and specific role for EMAP II in cardiac muscle. Moreover, the data of Schwarz et al. strongly suggested a role for EMAP II as a director of *neovascularization* in the developing lung, however it was concluded that *further experimentation* was required to determine the role of EMAP II in the control of vascular growth in adulthood (see concluding paragraphs on page L374). In other words, there was no clear guidance given in the prior art for the use of antibodies targeting EMAP II in cardiac muscle cells,

particularly for the facilitation of vascular growth *in vivo,* and further in an adult human patient suffering from a cardiac disorder.

Moreover, the disclosure of the Thompson et al. reference suggested that the biologically active form of EMAP II is not consistent in all mammals. Thompson et al. suggested that EMAP II can be found in two forms the mature and proforms, however it appears that the mature form (i.e. 21kDa) form is only expressed transiently, and the exact mechanism that controls the processing of the proform (i.e. 34 kDa) are unknown. Moreover, the above passage suggests that the manner in which EMAP II is processed may vary from one tissue type to the next, suggesting that different forms of the protein my control of regulate different activities in specific tissue types. Although Applicants noted that Thompson et al. teaches that EMAP II is expressed 6-week following myocardial infarction, it is unclear if the EMAP II that is referred to by Thompson et al. corresponds to the EMAP II of SEQ ID NO: 4 recited in the instant claims. (*Clarification of this point would be helpful.)*

Additionally, it was well known in the art that teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See Stryer et al.)

Therefore, Applicant's disclosure of a rabbit antibody to EMAP II, or an antibody targeting the amino acid sequence DAFPGEPDKELNP is insufficient since the overall structure of the biologically active form of EMAP II appears to be potentially variable from species to species, and from tissue type to tissue type.

Therefore, in view of the breadth of the claimed invention, the limited guidance in the specification as filed, and furthermore the lack of clarity in regards to the structure of biologically active EMAP II (as of the filing date of the instant application) targeted in the methods which read on treating any subject, human or otherwise, Applicants have not taught the skilled artisan how to practice the full scope of the claimed invention without undue experimentation.

9. The rejection of claims 1-4, 6-14, and 16-19 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in response to Applicant's arguments. However, the withdrawal of this rejection is not an admission that Applicants taught how to use the full scope of antibodies targeting SEQ ID NO: 4, or that the disclosure of antibodies targeting SEQ ID NO: 4 addresses the issue raised above in regards to the use of antibodies targeting the biologically active form of EMAP II.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE